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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/437,450	11/10/1999	JONATHAN H. FREEDMAN	1579-315	7992

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EXAMINER	
PRIEBE, SCOTT DAVID	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 07/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/437,450	FREEDMAN ET AL.	
	Examiner	Art Unit	
	Scott D. Priebe	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-19* is/are pending in the application.

4a) Of the above claim(s) *17-19* is/are withdrawn from consideration.

5)☒ Claim(s) *5-12* is/are allowed.

6)☒ Claim(s) *13-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 March 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20040322*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Group and/or Art Unit designation of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Primary Examiner Scott D. Priebe, Ph.D., Group Art Unit 1632.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The preliminary amendment filed 11/10/99 directing entry of the priority claim into the specification has been entered. The rejection of claims 7 and 11 under 35 USC 101 and 112, 1st para. has been withdrawn. Applicant argues that the specification at page 12 teaches monitoring expression of cadmium-responsive mRNAs in nematodes, and the specification shows that increased levels of mRNA corresponding to DDRT16 are produced in *C. elegans* in response to cadmium. It would have been readily apparent to one of skill in the art that nucleic acid comprising SEQ ID NO: 40 (or SEQ ID NOs: 14, 34 and 50) could be used as a probe to measure the level the corresponding mRNA expressed in *C. elegans* exposed to biological samples in an assay to detect cadmium in a sample.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to

37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 3/15/04 has been entered.

Election/Restrictions

Claims 17-19 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 3/4/03.

The restriction requirement filed 12/4/01 and Applicant's request for reconsideration of the restriction between Groups I-IV have been reviewed. Applicant's supporting material and argument that SEQ ID NOs: 14, 34, 40 and 50 are substantially the same sequence and that there would be no search burden in examining Groups I-IV are convincing. Groups I-IV are hereby rejoined.

Drawings

New corrected drawings are required in this application because the copies of the photographs in Figs. 1 and 3A & B are too dark to make out any detail. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Specification

The disclosure is objected to because of the following informalities: The paragraph beginning on page 7, line 2, last amended 4/12/02, has been replaced with the paragraph filed 3/15/04. The new amendment to this description of Fig. 5 (Figs. 5A-1 through 5A-39) removes the identification of the nucleotide sequences shown in the figures, which had been added in the 4/12/02 amendment. Consequently, the specification again fails to comply with 37 CFR 1.821(d). Furthermore, the amendment is improper under 37 CFR 1.121 since the amended paragraph does not indicate deletion of text, e.g. by strike-through, that had been present in this paragraph as of the amendment of 4/12/02.

Appropriate correction is required.

Claim Objections

Claims 13, 14, and 16 are objected to because of the following informalities: "genone" is misspelled and should be --genome--. Appropriate correction is required.

Claim Rejections - 35 USC § 101 & 112

Claim 15 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claim 15 is directed to a *C. elegans* engineered to differentially express the F35E8.11 gene product. However, as clearly shown in the specification, naturally occurring *C. elegans* already have the F35E8.11 gene, and the gene is differentially expressed at least in response to cadmium. The claim does not specify the nature of the "engineering" or

specify any material change to a naturally occurring *C. elegans* that would distinguish the "engineered" *C. elegans* from a naturally occurring one.

Claims 13, 14 and 16 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility.

Claims 13, 14, and 16 are directed to a *C. elegans* whose genome has been engineered to include a nucleic acid comprising SEQ ID NOs: 34, 50, or 14, respectively, each of which are partial cDNAs made from mRNA of the same gene. As indicated below, the subject matter of these claims is new matter. Thus, there is no assertion of utility for the claimed *C. elegans* in the original specification, nor is there any evidence of record for a well-established utility for the claimed subject matter.

The nucleic acids comprising SEQ ID NOs: 14, 34, and 50 could be used as probes in a biomonitor assay to detect changes in expression of the corresponding gene, the expression of which increases in response to cadmium in wild-type *C. elegans*, as indicated above. However, the claimed *C. elegans* have no such use.

The *C. elegans* generally described on page 13 as biomonitors have the structural gene (coding sequence) of a cadmium-responsive gene with that of a reporter protein. In essence, replacing the structural gene with that of a reporter protein, such as β-galactosidase or green fluorescent protein, makes expression from the promoter of the cadmium-responsive gene easier to monitor than doing Northern blots to measure mRNA levels. However, the rejected claims are not directed to an engineered *C. elegans* such as described on page 13, 1st para. Page 13 also describes engineering plants to overexpress a cadmium-responsive gene that encodes a protein

that functions in detoxification or in repair of cellular damage, so that the plants may grow in contaminated environments. However, the specification does not teach engineered *C. elegans* to this end, nor does it indicate that SEQ ID NOs: 34, 50, or 14 encode such a protein or that their overexpression would provide cadmium resistance.

Claims 13, 14 and 16 also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 13-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is reminded of their burden to indicate where and how amendments are supported by the original disclosure. See MPEP 714.02, last sentence of the third paragraph from the end and 2163.06 (I) last sentence.

Claims 13, 14, and 16 are directed to a *C. elegans* whose genome has been engineered to include a nucleic acid comprising SEQ ID NOs: 34, 50, or 14, respectively, each of which are partial cDNAs made from mRNA of the same gene. Applicants have pointed to Fig. 5, original claim 4, pages 13-14, and Table II of the specification for support of these claims (amendment filed 8/2/02). Claim 15 is directed to a *C. elegans* engineered to differentially express the

F35E8.11 gene product. Applicant has not indicated where or how the original specification supports this claim.

Original claim 4 does not provide support for the claimed *C. elegans*. Claim 4, is directed to a *C. elegans* whose genome comprises a cadmium-responsive gene while the instantly claimed C. elegans has a genome that comprises the nucleotide sequence set forth in SEQ ID NO: 34, 50, or 14. A cadmium-responsive gene is a broad recitation encompassing the entire genus of cadmium-responsive genes but does not necessarily support individual species within the genus. Moreover, a partial cDNA sequence is not a gene. Therefore, the recitation of cadmium-responsive gene does not support the nucleotide sequence set forth in SEQ ID NOs: 34, 50, or 14. With respect to claim 15, *C. elegans* already contains the F35E8.11 gene, and expresses the F35E8.11 gene product differentially is response to cadmium. Original claim 4 does not indicate adding this particular gene. Claim 15 is not directed to adding a gene, but to engineering *C. elegans* to differentially express the F35E8.11 gene product in some unspecified manner. Claim 15 would encompass making targeted mutations in the promoter of an endogenous F35E8.11 gene, for example.

The specification on pages 13-14 discusses transgenic organisms, particularly *C. elegans*, the genome of which has been engineered to include a cadmium-responsive gene. However, the discussion on pages 13-14 does not mention SEQ ID NOs: 34, 50, or 14 and is limited to general recitations of cadmium-responsive genes. Furthermore, page 13 generally describes replacing the structural gene (coding sequence) of a cadmium-responsive gene with that of a reporter protein to produce an organism that is a biomonitor. It also generally describes transgenic organisms, particularly plants, that overexpress "certain" cadmium-responsive genes that encode

proteins that function in detoxification or in repair of cellular damage. The specification does not identify a protein encoded by SEQ ID NOs: 34, 50, or 14, nor does it teach that any such protein has a function in detoxification or in repair of cellular damage, nor does it teach to engineer *C. elegans* to this end. Finally, page 13-14 generally describes knocking out cadmium responsive genes in a mammal, which does not pertain to the claimed subject matter. Thus, the discussion on pages 13-14 of the specification relating to transgenic organisms does not support a transgenic *C. elegans* whose genome comprises the nucleotide sequence set forth in SEQ ID NOs: 34, 50, or 14, or engineering *C. elegans* to differentially express the F35E8.11 gene product, which it already does.

Finally, Table II on pages 26-27 does not relate to transgenic *C. elegans*. Table II shows the various species of differentially expressed mRNAs isolated from wild-type *C. elegans* exposed to cadmium. Fig. 5 provides support only for SEQ ID NOs: 34, 50, or 14 themselves, not for an engineered *C. elegans*.

Claim 15 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 15 is directed to a *C. elegans* engineered to differentially express the F35E8.11 gene product. As indicated above, this subject matter was not described in the original specification. The claim is broadly directed to a C. elegans engineered in any way to differentially express, under any conditions, an F35E8.11 gene product. As disclosed in the

specification, the F35E8.11 gene is differentially expressed in wild-type *C. elegans* in response to cadmium. The claim does not restrict the differential expression to a cadmium response. The claim embraces differential expression in response any stimulus of interest, e.g. light, estrogen, bacterial prey, etc. It also embraces any change in the genome of *C. elegans* that would lead to the differential expression.

The specification must teach those of skill in the art how to make and how to use the invention as broadly claimed. *In re Goodman*, 29 USPQ2d at 2013 (Fed. Cir. 1994), citing *In re Vaeck*, 20 USPQ2d at 1445 (Fed. Cir. 1991). The specification provides no guidance on how to make a single engineered *C. elegans* readable on the claim, nor does it provide a single working example of such. The specification does not disclose or describe a F35E8.11 gene product or gene, any promoter sequence that could be used to effect the differential expression, nor any mutation of an endogenous F35E8.11 gene that would alter the differential expression characteristic of the F35E8.11 gene. In short, it is left entirely for one of skill in the art to find out for themselves what materials are needed for the engineering and what specific changes to engineer. With the exception of using such a *C. elegans* as a biomonitor for cadmium, the specification does not teach how to use the claimed *C. elegans* wherein the differential expression is not in response to cadmium.

A patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion. Tossing out the germ of an idea does not constitute an enabling disclosure. While every aspect of a generic claim need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable the skilled artisan to understand and carry out the invention. It is true that a specification need not

disclose what is well known in the art. However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. The rule that a specification need not disclose that which is well known in the art simply means that omission of minor details does not cause a specification to fail the enablement requirement, and is not a substitute for an enabling disclosure. However, if there is no disclosure of starting materials and of conditions under which the process can be carried out, undue experimentation is required. Failure to provide such teachings cannot be rectified by asserting that the disclosure of the missing necessary information was well known in the prior art. See *Genentech Inc. v. Novo Nordisk A/S*, 42 USPQ2d 101, 1005 (CA FC, 1997). Due to the complete lack of guidance and working examples in the original specification, as well as the lack of description for the claimed *C. elegans*, it would clearly require one of skill in the art to engage in inventive activity and undue experimentation in order to practice any embodiment of the claimed invention, much less practice the invention as broadly as it is claimed.

Claim Rejections - 35 USC § 102

Claim 15 is rejected under 35 U.S.C. 102(b) as being anticipated by Freedman et al. (J. Biol. Chem. 268 (4): 2554-2564, 1993).

Claim 15 is directed to a *C. elegans* engineered to differentially express the F35E8.11 gene product. However, as clearly shown in the specification, *C. elegans* inherently has the F35E8.11 gene, and the gene is differentially expressed at least in response to cadmium. Freedman discloses the N2 laboratory strain of *C. elegans* (e.g. page 2555, col. 2) described in the instant specification as differentially expressing the F35E8.1 gene. The claim does not

specify the nature of the "engineering" or specify any material change to *C. elegans* strain N2, for example, that would distinguish the "engineered" *C. elegans* from N2.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. GenBank Acc. No. Z81529 (21 Sep. 1998 version) is the closest prior art. Nucleotides 14-30 of SEQ ID NO: 40 are identical to nucleotides 18456-18572 (3' end of predicted penultimate coding exon) and nucleotides 31-225 of SEQ ID NO: 40 are identical to nucleotides 18626-18820 (includes 3' end of coding sequence) except for a single mispair at nucleotides 218 and 18813 of SEQ ID NO: 40 and Z81529, respectively. Nucleotides 14-225 of SEQ ID NO: 40 are identical to part of the predicted mRNA sequence from Z81529 (except for the mispair). Nucleotides 1-13 and 226-238 diverge from the corresponding sequences in Z81529. SEQ ID NO: 40 has the highest sequence identity to Z81529. SEQ ID NOs: 14, 34 and 50 diverge from SEQ ID NO: 40 and Z81529. Neither the genomic DNA nor predicted mRNA from Z81529 would include SEQ ID NO: 40, or any of SEQ ID NOs: 14, 34 or 50, which were made from mRNA from the same source as that of SEQ ID NO: 40. Except for the mispair mentioned above, the sequence differences between each of SEQ ID NO: 14, 34, 40, and 50 and between these and Z81529 suggests that the claimed nucleic acids have a synthetic sequences that include artifactual nucleotide differences introduced by the cloning process or due to sequencing errors. The nucleotide at position 218 of SEQ ID NO: 40 is identical to the corresponding nucleotide in each of SEQ ID NOs: 14, 34, and 50, which suggests that this nucleotide position is polymorphic in nature.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe whose telephone number is (571) 272-0733. The examiner can normally be reached on M-F, 8:00-4:00. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy J. Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Scott D. Priebe
Primary Examiner
Art Unit 1632